

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 07 August 2000 (07.08.00)	
International application No. PCT/US99/27465	Applicant's or agent's file reference 19452-3-2PC
International filing date (day/month/year) 20 November 1999 (20.11.99)	Priority date (day/month/year) 21 November 1998 (21.11.98)
Applicant. MARTH, Jamey, D. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
20 June 2000 (20.06.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

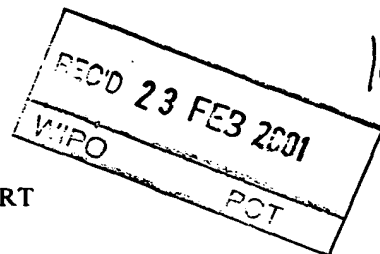
<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer Juan Cruz</p> <p>Telephone No.: (41-22) 338.83.38</p>
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 19452-3-2PC	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/27465	International filing date (day/month/year) 20 NOVEMBER 1999	Priority date (day/month/year) 21 NOVEMBER 1998
International Patent Classification (IPC) or national classification and IPC IPC(6): and US Cl.:		
Applicant THE REGENTS OF THE UNIVERSITY OF CALIFORNIA		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

I ☒ Basis of the report

II ☐ Priority

III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability

IV ☐ Lack of unity of invention

V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

VI ☒ Certain documents cited

VII ☐ Certain defects in the international application

VIII ☐ Certain observations on the international application

Date of submission of the demand 20 JUNE 2000	Date of completion of this report 12 JANUARY 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer Jane Zera
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/27465

I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain*

☒ the international application as originally filed.

☒ the description, pages 1-51, as originally filed.

pages NONE, filed with the demand.

pages NONE, filed with the letter of _____.

pages _____, filed with the letter of _____.

☒ the claims, Nos. 1-35, as originally filed.

Nos. NONE, as amended under Article 19.

Nos. NONE, filed with the demand.

Nos. NONE, filed with the letter of _____.

Nos. _____, filed with the letter of _____.

☒ the drawings, sheets/fig 1-6, as originally filed.

sheets/fig NONE, filed with the demand.

sheets/fig NONE, filed with the letter of _____.

sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☒ the description, pages NONE.

☒ the claims, Nos. NONE.

☒ the drawings, sheets/fig NONE.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/27465

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

Novelty (N)	Claims	<u>7, 18-20, 24-35</u>	YES
	Claims	<u>1-6, 8-17, 21-23</u>	NO
Inventive Step (IS)	Claims	<u>24-35</u>	YES
	Claims	<u>7, 18-20</u>	NO
Industrial Applicability (IA)	Claims	<u>1-35</u>	YES
	Claims	<u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-6 and 8-17 lack novelty under PCT Article 33(2) as being anticipated by Wong et al.

Wong et al teach inhibitors of glycosyl transferases, which transferases include beta-6 N-acetylglucosaminyl transferase.

Claims 1-6, 8-13 and 17 lack novelty under PCT Article 33(2) as being anticipated by Toki et al.

Toki et al teach nitrophenyl substrate inhibitors to beta-6 N-acetylglucosaminyl transferase.

Claims 1-18 lack novelty under PCT Article 33(2) as being anticipated by Nakamura et al.

Nakamura et al teach phorbol ester inhibition of beta-6 N-acetylglucosaminyl transferase.

Claims 1-6 and 8-17 lack novelty under PCT Article 33(2) as being anticipated by Vaghefi et al.

Vaghefi et al teach glycopyranosylphosphonate analogues of nucleoside diphosphate sugars as inhibitors of beta-6 N-acetylglucosaminyl transferase.

Claims 1-6, 8-17 and 21-23 lack novelty under PCT Article 33(2) as being anticipated by Fukuda et al.

Fukuda et al teach the cloning, characterization and expression of human beta-6 N-acetylglucosaminyl transferase, and active fragments thereof, which enzyme forms core 2 oligosaccharide structures in O-glycans. Fukuda et al also teach antibodies targeting this enzyme, mutations and inactive fragments which inhibit the enzyme's activity.

Claims 7 and 18-20 lack an inventive step under PCT Article 33(3) (Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/27465

VI. Certain documents cited**1. Certain published documents (Rule 70.10)**

<u>Application No. Patent No.</u>	<u>Publication Date (day/month/year)</u>	<u>Filing Date (day/month/year)</u>	<u>Priority date (valid claim) (day/month/year)</u>
5,880,091	09 MARCH 1999	07 JUNE 1995	16 NOV 1992
5,843,707	01 DEC 1999	25 APRIL 1995	23 OCT 1992

2. Non-written disclosures (Rule 70.9)Kind of non-written disclosureDate of non-written disclosure
(day/month/year)Date of written disclosure
referring to non-written disclosure
(day/month/year)

Supplemental B x

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

as being obvious over the prior art as applied in the immediately preceding paragraph and further in view of Milner et al and James. Fukuda et al disclose nucleic acid sequences encoding beta-6 N-acetylglucosaminyl transferase. Milner et al and James both teach methods of selecting effective antisense reagents for inhibiting the expression of a target gene of known sequence.

Claims 24-35 the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest methods of identifying compounds which inhibit an inflammatory response in a mammal comprising the determination of a modulation in core 2 Glc NAc activity.

----- NEW CITATIONS -----

none



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Eingangs-
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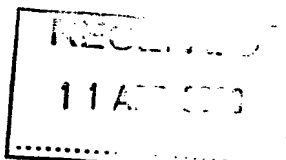
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Pat nt Office

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Office européen
des brevets

Section de
Dépôt

Brasnett, Adrian Hugh
Mewburn Ellis
York House
23 Kingsway
London WC2B 6HP
GRANDE BRETAGNE



Datum/Date

09-04-2003

Zeichen/Ref./Ref. AHB/FP5927264	Anmeldung Nr./Application No./Demande n°./Patent Nr./Patent No./Brevet n°. 99959043.3-2110- PCT/US9927465
Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire The Regents of the University of California	

PROCEEDING FURTHER WITH THE EUROPEAN PATENT APPLICATION PURSUANT TO
ARTICLE 96(1) AND RULE 51(1) EPC

A supplementary European search report has been drawn up concerning
the above European patent application (publication no. 1131334).

Since you have filed a request for examination prior to the trans-
mission of the supplementary European search report, you are hereby
invited to indicate within

TWO MONTHS

of notification of this invitation whether you desire to proceed
further with the European patent application.

If you do not indicate in due time that you desire to proceed further
with the European patent application, it will be deemed to be withdrawn
(Art. 96(3) EPC).

If you wish you may comment on the supplementary European search report
and amend, where appropriate, the description, claims and drawings
(Rule 51(1) EPC).

RECEIVING SECTION

19/6/03	ENTD FOR
MAR	AHB
AHB	2.



REGISTERED LETTER

EPO Form 1224 04.85

7001007 29/03/03

99959043.3 DMEX

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Europäisches
Patentamt

Zweigstelle
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Département à
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Division de la
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Brasnett, Adrian Hugh
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- 3 APR 2003

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ALREADY ENTERED

Datum/Date

03.04.03

Zeichen/Ref./Ref

AHB/FP5927264

Anmeldung Nr./Application No./Demande n°/Patent Nr./Patent No./Brevet n°

99959043.3-2110-US9927465

Anmelder/Applicant/Demandeur Patentinhaber/Proprietor/Titulaire

The Regents of the University of California

COMMUNICATION

The European Patent Office herewith transmits as an enclosure the European search report for the above-mentioned European patent application.

If applicable, copies of the documents cited in the European search report are attached.

☒ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

REFUND OF THE SEARCH FEE

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.



DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	WO 97 06176 A (UNIV OKLAHOMA STATE ;MOORE KEVIN L (US); MCEVER RODGER P (US); CUM) 20 February 1997 (1997-02-20) * the whole document *	1-23, 32-35	C07H21/04 C07K16/00 C12N15/63 C12N15/85 A61K48/00 C12N15/11 C12Q1/48
X	MAAHEIMO, HANNU ET AL: "Synthesis of a divalent sialyl Lewis x O-glycan, a potent inhibitor of lymphocyte-endothelium adhesion. Evidence that multivalency enhances the saccharide binding to L-selectin" EUROPEAN JOURNAL OF BIOCHEMISTRY (1995), 234(2), 616-25 , XP000613069 * the whole document *	1-23	
X	JAIN, RAKESH K. ET AL: "Inhibition of L- and P- selectin by a rationally synthesized novel core 2 -like branched structure containing GalNAc-Lewisx and Neu5Ac.alpha.2-3Gal.beta.1-3GalNAc sequences" GLYCOBIOLOGY (1998), 8(7), 707-717 , XP001011268 * the whole document *	1-23	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
			C12N C12Q A61K
X	CA 2 186 987 A (MOUNT SINAI HOSPITAL CORP) 2 April 1998 (1998-04-02) * the whole document *	24-31	
X	HINDSGAUL, OLE ET AL: "Evaluation of deoxygenated oligosaccharide acceptor analogs as specific inhibitors of glycosyltransferases" JOURNAL OF BIOLOGICAL CHEMISTRY (1991), 266(27), 17858-62 , XP000999205 * claim 2; table I *	24-31	
	-/--		
	The supplementary search report has been based on the last set of claims valid and available at the start of the search.		
	Place of search MUNICH	Date of completion of the search 18 March 2003	Examiner Bardili, W
CATEGORY OF CITED DOCUMENTS		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			



DOCUMENTS CONSIDERED TO BE RELEVANT															
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)												
P,X	ELLIES, LESLEY G. ET AL: "Core 2 oligosaccharide biosynthesis distinguishes between selectin ligands essential for leukocyte homing and inflammation" IMMUNITY (1998), 9(6), 881-890 , XP002235083 * the whole document * -----	1-35													
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)												
The supplementary search report has been based on the last set of claims valid and available at the start of the search.															
Place of search MUNICH		Date of completion of the search 18 March 2003	Examiner Bardili, W												
<table border="0"><tr><td>CATEGORY OF CITED DOCUMENTS</td><td></td></tr><tr><td>X : particularly relevant if taken alone</td><td>T : theory or principle underlying the invention</td></tr><tr><td>Y : particularly relevant if combined with another document of the same category</td><td>E : earlier patent document, but published on, or after the filing date</td></tr><tr><td>A : technological background</td><td>D : document cited in the application</td></tr><tr><td>O : non-written disclosure</td><td>L : document cited for other reasons</td></tr><tr><td>P : intermediate document</td><td>& : member of the same patent family, corresponding document</td></tr></table>				CATEGORY OF CITED DOCUMENTS		X : particularly relevant if taken alone	T : theory or principle underlying the invention	Y : particularly relevant if combined with another document of the same category	E : earlier patent document, but published on, or after the filing date	A : technological background	D : document cited in the application	O : non-written disclosure	L : document cited for other reasons	P : intermediate document	& : member of the same patent family, corresponding document
CATEGORY OF CITED DOCUMENTS															
X : particularly relevant if taken alone	T : theory or principle underlying the invention														
Y : particularly relevant if combined with another document of the same category	E : earlier patent document, but published on, or after the filing date														
A : technological background	D : document cited in the application														
O : non-written disclosure	L : document cited for other reasons														
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1
EPO FORM 1503 03 82 (P04C04)

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 99 95 9043

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

18-03-2003

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9706176	A	20-02-1997	AU	723262 B2	24-08-2000
			AU	6766996 A	05-03-1997
			CA	2228512 A1	20-02-1997
			EP	0850243 A2	01-07-1998
			JP	11510543 T	14-09-1999
			US	6124267 A	26-09-2000
			WO	9706176 A2	20-02-1997
<hr/>					
CA 2186987	A	02-04-1998	CA	2186987 A1	02-04-1998
<hr/>					



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07H 21/04, C07K 16/00, C12N 15/63, 15/85, A61K 48/00	A1	(11) International Publication Number: WO 00/31109 (43) International Publication Date: 2 June 2000 (02.06.00)
(21) International Application Number: PCT/US99/27465 (22) International Filing Date: 20 November 1999 (20.11.99) (30) Priority Data: 60/109,416 21 November 1998 (21.11.98) US 60/113,679 21 December 1998 (21.12.98) US (71) Applicant (for all designated States except US): THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US/US]; 12th floor, 1111 Franklin Street, Oakland, CA 94607 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): MARTH, Jamey, D. [US/US]; 7190 Shoreline Drive, San Diego, CA 92122 (US). ELLIES, Leslie, G. [US/US]; 3295 Caminito East Bluff #188, La Jolla, CA 92037 (US). (74) Agents: SMITH, Timothy, L. et al.; Townsend and Townsend and Crew LLP, 8th Floor, Two Embarcadero Center, San Francisco, CA 94111-3834 (US).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: USE OF CORE 2 GlcNAc TRANSFERASE INHIBITORS IN TREATING INFLAMMATION (57) Abstract This invention provides compounds and methods for treating inflammation. The compounds modulate the core 2 oligosaccharide-mediated binding of inflammatory cells, such as neutrophils, to endothelial cells and other myeloid cells. Significantly, the of the invention methods block inflammation without affecting lymphocyte trafficking. In some embodiments, the compounds inhibit the activity of a core 2 GlcNAc transferase that is involved in synthesizing the core 2 oligosaccharides.		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/27465

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :C07H 21/04;C07K 16/00;C12N 15/63 15/85;A61K 48/00

US CL : 536/23.1 24.5 25.3;514/44;435/320.1 455;530/387.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1, 24.5, 25.3;514/44;435/320.1, 455;530/387.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

West, Dialog

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	US 5,843,707 A (LARSEN et al.) 01 December 1998, see abstract and columns 3-4.	1,2,9-13,32-35
X,P	US 5,880,091 A (CUMMINGS ET AL)09 March 1999, abstract, col. 4, Line 49-col. 17, Line 57.	1,2,9-13,32-35.
X	VAGHEFI, MM ET AL. synthesis of glycopyranosylphosphonate analogues of certain natural nucleoside diphosphate sugars as potential inhibitors of glycosyltransferases j.Med.Chem 1987, vol 30, pages 1383-1391.	1-6,8-17,24-31
X	VAGHEFI M.M. ET AL. synthesis of certain nucleoside methylenediphosphonate sugars as potential inhibitors of glycosyltransferases j.Med.Chem. 1987 Vol. 30, Pages 1391-1399.	1-6,8-17,24-31.

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

11 FEBRUARY 2000

Date of mailing of the international search report

29 FEB 2000

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Washington, D.C. 20231

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Authorized officer

Jane Zara

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/27465

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,461,143 (WONG ET AL)24 October 1995, abstract,col.1,Lines 24-27,col. 6, Line 50-col. 21, Line 16. Table 2.	1-6,8-17,24-31.
X	NAKAMURA M. ET AL. single glycosyltransferase, core 2 beta 1-6 n-acetylglycosaminyltransferase, regulates cell surface sialyl le(x) expression level in human pre-b lymphocytic leukemia cell line km3 treated with phorbol ester 1998 vol 273. No 41. Pages 26,779-26,789, see Entire text.	1-18,24-31
X	TOKI D. ET AL. inhibition of udp-glcnac-r beta6-n-acetylglucosaminyltransferase from acute myeloid leukaemia cells by photoreactive nitrophenyl substrate derivatives. Biochem. Biophys. Res. Comm. Vol. 198. No. 2. Pages 417-423, see Entire text.	1-6,8-13,17,24-31.
X	US 5,360,733 (FUKUDA ET AL) 01 November 1994, abstract, col.4,Line 67-col 5, line 7, col8, line 40-col 9,line 64, col 10, line 45-col 11, line 7.	1-35
Y	MILNER M ET AL. SElecting effective antisense reagents on combinatorial oligonucleotide arrays. Nature june 1997. Vol. 15. Pages 537-541. Entire text.	1-7,9-16,18 -20
Y	JAMES W. towards gene-inhibition therapy: a review of progress and prospects in the field of antiviral antisense nucleic acids and ribozymes. Antiviral chem. And chemother. 1991. Vol. 2. No. 4. Pages 191-214. Especially pages 197-198.	1-7,9-16,18-20.